Attorney's Docket No. US-146O

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	
IMAIZUMI et al.	Art Unit: 1652
Application No.: 10/023,711	Examiner: Christian L. Fronda
Filing Date: December 21, 2001	Attorney Ref. No.: US-146O
For: METHOD OF PRODUCING TARGET SUBSTANCE BY FERMENTATION	Confirmation No.: 6895

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
Alexandria, Virginia 22313

Sir:

In response to the Non-Final Official Action dated November 9, 2007, issued in response to the Interview of September 25, 2007, Applicant herewith files a Notice of Appeal and requests a Pre-Appeal Brief Review in accordance with the guidelines set forth in the July 12, 2005 Official Gazette Notice. The claims have been twice rejected, and therefore appeal and this pre-appeal brief request are timely. Reconsideration of this application by a three Examiner panel is requested in view of the following remarks which identify the errors in facts, and the omission of essential elements required to establish a *prima facie* rejection.

Summary of Previous Office Action and Status of Case

In the non-final Office Action mailed November 9, 2007, Claims 1, 7-10, and 12-14 stand rejected under 35 U.S.C. §112, 1st paragraph, as allegedly the specification does not provide enablement for the production of an L-amino acid other than L-lysine, L-glutamic acid, and L-tryptophan. The claims were rejected under this statute and for this reason in the Office Action issued August 10, 2006, the Final Office Action issued January 29, 2007, and the most recent non-final Office Action issued on November 9, 2007. As the claims have been at least twice rejected under this section, this appeal and this pre-appeal request are

timely filed. Claims 6 and 11 are objected to as being dependent on a rejected base claims, but otherwise are allowable. Claims 2-5 were cancelled.

Summary of Claimed Invention

The claimed invention is directed to a method for producing an L-amino acid comprising culturing an *Escherichia coli* bacterium in a medium, allowing said L-amino acid to accumulate in the medium and/or in the cells of the bacterium, and collecting said L-amino acid, wherein the endogenous *Escherichia coli* gene encoding the RMF protein is mutated so that the RMF protein is inactive, and wherein said L-amino acid is produced in larger quantities than if the RMF protein were active.

Factual Errors Requiring Review

The claims stand rejected on the grounds that the specification is allegedly only enabling under 35 U.S.C. §112, 1st paragraph for a method for producing L-lysine, L-glutamic acid, and L-tryptophan using an *E. coli* bacterium whose endogenous RMF protein is mutated so that the RMF protein is inactive.

As described in Examples 2 and 3 of the specification and the Declarations under 37 C.F.R. §1.132 submitted on March 28, 2005 and May 5, 2006, the disruption and concomittant inactivation of the *rmf* gene improved production of L-lysine, L-glutamic acid, and L-typtophan. Also, as shown in these examples and the Declarations, disruption of the *rmf* gene improved bacterial growth. In particular, the production of L-lysine (example 2 in the specification), L-glutamic acid (March 28, 2005 declaration), and L-tryptophan (May 5, 2006 declaration) can be increased by inactivation of the RMF protein. These exemplified amino acids are very diverse, and represent very different structures, demonstrating a wide range of the claimed genus production method. Specifically, such data exemplifies production of basic (L-lysine), acidic (L-glutamic acid), and aromatic (L-tryptophan) amino acids, demonstrating the application of the claimed method to different kinds of amino acids. Most notably, success of the claimed method among these three diverse types of amino acids clearly demonstrates that extrapolating the method to other non-exemplified amino acids would be well within the skill of the ordinarily-skilled art worker without undue experimentation. Therefore, production of any amino acid is sufficiently supported and enabled.

It is well known in the field of bacterial fermentation that the production of L-amino acids by bacteria depends on the ability of the bacteria to produce L-amino acids per unit of bacterial mass. Therefore, improving the growth of the bacteria will lead to improved production of any L-amino acid. It is also known in the art that many strains of *E. coli* are able to produce various L-amino acids.

Therefore, one of ordinary skill in the art would be able to determine the productivity of L-amino acids in other know bacterial strains, particularly those known to produce L-amino acids other than L-lysine, L-glutamic acid, and L-tryptophan, based upon the working examples provided regarding mutating the endogenous RMF protein so that the RMF protein is inactive in known *E. coli* strains. Thus, production of L-amino acids other than L-lysine, L-glutamic acid, and L-tryptophan, is enabled. No undue experimentation is required since *E. coli* bacterial strains are known for producing any L-amino acid, and the specification clearly teaches that inactivation of the RMF gene will improve bacterial growth and increase production of the L-amino acid known to be produced in the chosen strain.

Furthermore, the genus of L-amino acids is fairly small in that there are only 20 known naturally occuring L-amino acids. These molecules are all fairly small and similar in their structure and function, although some are known to be basic, acidic, branched chain, or cyclical. The three exemplified L-amino acids in the present specification and Declarations represent several of these various groups in that L-glutamic acid is acidic, L-lysine is basic, and L-tryptophan is cyclical. Such evidence is indicative of the method of the present invention being effective and expected to be effective by the person of ordinary skill in the art for a broad range of types of L-amino acids. Furthermore, exemplification of every embodiment is not required to satisfy 35 U.S.C. §112, 1st paragraph, and inoperative embodiments are permitted (*Altas Powder Co. v. E.I. duPont de Nemours and Co.*, 750 F.2d 1569, 1577 (Fed. Cir. 1984)).

In addition, as shown in the present specification (Fig. 1), and the Declaration which was submitted on March 28, 2005, disruption of the *rmf* gene of an *Ecsherichia* bacterium improved the growth of the bacterium ***in the stationary phase***. Furthermore, improving the production of L-amino acids in an *Escherichia* bacterium in which the *rmf* gene has been disrupted is due to the improved growth in the stationary phase, not because of the disruption of the *rmf* gene or any effect this might have on the specific biosynthetic pathway of a particular amino acid.

Therefore, one of ordinary skill in the art would be able predict that productivity of L-amino acids other than L-lysine, L-glutamic acid, and L-tryptophan in an *Escherichia coli* bacterium could be improved by mutating the endogenous RMF protein so that the RMF protein is inactive in known *E. coli* strains which have an ability to produce L-amino acid other than the three amino acids. Thus, production of L-amino acids other than L-lysine, L-glutamic acid, and L-tryptophan, is enabled.

For at least the foregoing reasons, Applicant respectfully submits that Claims 1, 7-10 and 12-14 fully comply with 35 U.S.C. § 112, first paragraph, and therefore respectfully requests withdrawal of the rejection thereof under 35 U.S.C. § 112.

Conclusion

In the interest of brevity, Applicant does not provide all arguments that would support an appeal for each of the pending and rejected claims. However, it is respectfully submitted that this case is in immediate and clear form for allowance based on the clear errors and omissions cited above. Accordingly, an early indication via a Notice of Allowability that all claims are allowable is respectfully requested. Should any questions arise in connection with this application or should the Examiner believe that a telephone conference with the undersigned would be helpful in resolving any remaining issues pertaining to this application, the undersigned respectfully requests that he be contacted at the number indicated below.

Respectfully submitted,

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